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10/678,145	10/06/2003	Walter C. Babcock	PC26122A	1094

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PATENT DEPARTMENT, MS8260-1611
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GROTON, CT 06340

EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	**PAPER NUMBER**
1616	

NOTIFICATION DATE	DELIVERY MODE
06/25/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

~IPGSGro@pfizer.com

Office Action Summary	Application No.	Applicant(s)	
	10/678,145	BABCOCK ET AL.	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/13/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4, 7-8, and 10-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-4, 7-8, and 10-15 are pending. Applicants have cancelled claims 5-6 and 9. Applicants have amended claim 1. Claim 15 is withdrawn as being drawn to a non-elected invention. Receipt and consideration of Applicants' amended claim set and remarks/arguments submitted on 13 February 2008 are acknowledged. All rejections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments. Applicants are advised that a different Examiner is examining the instant application.

Specification

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 2, from which claim 3, depends already claims that the composition further comprises a concentration-enhancing polymer. Specifying in claim 3 that component (a) of the composition further comprises said concentration-enhancing polymer does not further limit parent claim 2, because components (a) and (b) are part of the same composition and are understood as being admixed. Thus, if the composition further comprises a concentration-enhancing

polymer, then component (a) necessarily further comprises a concentration-enhancing polymer.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 7-8, 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sikorski et al. (WO 00/38722; "Sikorski", IDS reference) in view of Gurtler et al. (U.S. Patent No. 5,773,021; "Gurtler", of record), Mulligan et al. (U.S. Patent No. 5,128,142; "Mulligan", of record), and Rowe et al. (US 2003/0099708).

Applicant Claims

Applicants claim a composition comprising (a) a solid amorphous adsorbate comprising a cholesteryl ester transfer protein inhibitor (CETPI) that is (2R)-3-((4-(4-chloro-3-ethylphenoxy)phenyl)(3-(1,1,2,2-tetrafluoroethoxy)benzyl)amino)-1,1,1-trifluoro-2-propanol and is adsorbed onto a substrate, wherein the substrate surface has a surface area of at least 20 m2/g and 60% or more of the CETPI is amorphous (i.e. a "major portion" is amorphous, see definition of "major portion" in paragraph [1073] in specification) and (b) an HMG-CoA reductase inhibitor (e.g. atorvastatin). In some embodiments the composition further comprises a concentration-enhancing polymer (e.g. cellulose acetate trimellitate) and/or a dissolution enhancing polymer (e.g. PVP).

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Sikorski teaches combinations of an HMG CoA reductase inhibitor and CETP inhibitor (abstract) that are suitable for the treatment of cardiovascular disease. **The elected CETP inhibitor is specified ("C-12" on page. 18).** The elected atorvastatin is disclosed (Table 2 page 21). Specifically in Table 3 on page 38, Sikorski teaches **a composition comprising both the elected CETPI and atorvastatin.** Sikorski's claim 7

also specifies the combination of a CETPI with atorvastatin. **Tablets are specified (page 26, line 30).**

Gurtler teaches an insert polymeric material matrix for prolonged and control release in which a medicinal substance is incorporated (abstract). Adsorption onto a support is disclosed (column 3 lines 25-32) as an exemplified pre-treatment of the medicinal substrate. **Cellulose acetate trimellitate is specified** (column 3, line 46). Other suitable physical support polymers are also disclosed, including **various substituted neutral celluloses** and other polymers (col. 3, lines 41-54).

Mulligan et al teach a controlled release formation comprising **an active and an inactive substance *adsorbed* onto a cross-linked polymer** (abstract). The cross-linked polymer may be porous (col. 2, lines 10-13). The inactive substance may be water soluble to enhance the rate of active leached (column 2 lines 48-52). **Polyvinylpyrrolidone** is specified (column 3 lines 31-32), as a suitable inactive substance. (On page 123 line 25 applicants disclose polyvinylpyrrolidone as a preferred dissolution-enhancing agent.).

Rower teaches that it is know that **one method of increasing the bioavailability of an active pharmaceutical ingredient (API) is to alter its structure, and that amorphous API has greater aqueous solubility than the corresponding crystalline API**, and consequently a greater bioavailability. For example, it has been shown that an amorphous API can have a greater bioavailability of about a factor of 5 relative to the corresponding crystalline form of said API ([0033]).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Sikorski lacks the explicit teaching of amorphous drug, a composition in the form of an adsorbate, and compositions comprising concentration-enhancing or dissolution-enhancing polymers. These deficiencies are cured by the teachings of the combined prior art and what is commonly known in the art.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to modify the composition of Sikorski to adsorb the drug composition disclosed onto or into a cross-linked polymer to obtain the benefits of a controlled-release formulation taught by (Gurtler). The cross-linked polymer disclosed by Gurtler is identified by Applicants as being a concentration-enhancing polymer, thus, Sikorski's compositions as modified by the teachings of Gurtler would necessarily exhibit similar properties as Applicants' claims requiring a concentration-enhancing polymer. Furthermore, it would have been prima facie to also utilize polyvinylpyrrolidone in Sikorski's compositions to obtain the benefits of the sustained release formulations disclosed by Mulligan. Sustained release is a kind of controlled release. Polyvinylpyrrolidone is taught by Mulligan as being a suitable substrate onto or into which an API may be adsorbed. Applicants have identified PVP as a dissolution-enhancing polymer. Thus, Sikorski's compositions modified to comprise PVP would necessarily exhibit API dissolution enhancing properties due to the presence of PVP. It is noted that wherein polymers are used as the substrate onto which or into which an API is adsorbed, these substrates are often porous (e.g. Mulligan) and as such

would necessarily have a higher surface area than non-porous substrates. Regarding whether the active substance is in an amorphous form or a crystalline form, it is common knowledge in the art that the amorphous form of a given API will have a greater aqueous solubility than its crystalline form and consequently a greater bioavailability. Enhancing the bioavailability of an API is a desirable result, as improved bioavailability enables one to prepare compositions requiring a lower amount of drug (Rower), which lowers productions costs and costs to the consumer, as well as reduces the likelihood of undesirable side effects. Thus, it would have been prima facie obvious and desirable to adsorb an amorphous API, such as the API's present in Sikorski's composition, onto or into a polymer matrix comprising PVP and cellulose triacetate mellitate to obtain a composition exhibiting enhanced bioavailability, sustained release, and concentration enhancement properties. Although the combined references are silent as to the surface area of the substrate, it would have been common sense to optimize the surface area of a composition comprising a porous substrate having adsorbed therein or thereon an amorphous drug to optimize the dissolution properties and bioavailability of the API of said formulation. An ordinary skilled artisan would have had a reasonable expectation of successfully adsorbing Sikorski's drug formulations onto the substrate polymers taught by both Mulligan and Gurtler, because both the actives taught by Sikorski have low water solubility and the adsorption of low solubility drugs onto polymer surfaces is known (Gurtler and Mulligan) as a means of increasing bioavailability. Regarding the properties recited in claims 10 and 12, it is the Examiner's position that the compositions resulting from the teachings of the combined prior art and upon optimization of said teachings would necessarily exhibit the same or similar properties. Therefore, the claimed

invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 10, and 13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 11, 13-14, 33-34, 45, 65, and 67-68 of copending Application No. 10/173,987 (copending '987) in view of Sikorski et al. (WO 00/38722). Independent claim 1 of the instant application has been described supra. Independent claim 1 of copending '987 claims a pharmaceutical composition comprising a solid adsorbate comprising a low solubility drug, wherein the substrate is selected from a group consisting of silica, titania,

zinc oxide, and alumina and the drug is at lest 80% amorphous. Independent claim 2 of copending '987 claims a similar pharmaceutical composition as claim 1 of copending '987 and further specifies that the substrate as a surface area of at lest 20 m^2/g and the composition also comprises a concentration-enhancing polymer. Dependent claims 33-34 of copending '987 further specify that the claimed compositions comprise a concentration-enhancing polymer selected from various neutral and ionizable cellulosic polymers. Dependent claim 65 identifies PVP as a suitable concentration-enhancing polymer as well, and PVP is necessarily a dissolution-enhancing polymer too, because it has been identified by Applicants as being a dissolution-enhancing polymer. Dependent claim 68 of copending '987 specifies that the drug is the same CETPI recited in the claims of the instant application. The claims of copending '987 are silent as to the presence of a HMG-CoA reductase inhibitor (e.g. atorvastatin). This deficiency is cured by the teachings of Sikorski, which establishes that both CETPI and HMG-CoA reductase inhibitors are known to be indicated for the treatment of the same conditions and are known in combination. There would have been a reasonable expectation of successfully formulating a HMG-CoA reductase inhibitor with a CETPI, because this combination is known in the prior art. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 1-4, 10, and 13 *prima facie* obvious over claims 1-2, 11, 13-14, 33-34, 45, 65, and 67-68 of copending Application No. 10/173,987 (copending '987) in view of Sikorski et al. (WO 00/38722).

This is a provisional obviousness-type double patenting rejection.

Claims 1-4, 7-8, and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 9, 13-14, 23-24, and 31-32 of copending Application No. 10/739,750 (copending '750) in view of in view of Gurtler et al. (U.S. Patent No. 5,773,021; "Gurtler", of record) and Mulligan et al. (U.S. Patent No. 5,128,142; "Mulligan", of record). Independent claim 1 of the instant application has been described supra. Independent claim 1 of copending '750 claims a unitary dosage form comprising (a) a solid amorphous dispersion comprising the same CETPI recited in the claims of the instant application, (b) a concentration-enhancing polymer, and (c) a HMG CoA reductase inhibitor. Dependent claims 23-24 of copending '750 specify that the HMG CoA reductase inhibitor is selected from a group including atorvastatin and dependent claim 31 of copending '750 specifies that suitable forms of the composition include capsule, tablet, pill, powder, etc. The primary difference between the claims is that the claims of copending '750 do not specify that the CETPI is adsorbed onto a substrate and that the substrate has a specific surface area. This deficiency is cured by the teachings of Gurtler and Mulligan, which establish that adsorption of drugs onto or into a polymer substrate surface is a method suitable for making controlled release and sustained release formulations, which convey controlled release properties that advantageously require fewer dosings per day. Regarding the surface area deficiency, it would have been prima facie obvious to optimize the substrate surface area to control and modify the bioavailability of the adsorbed drug (i.e. more surface area = higher bioavailability for a given amorphous API). Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 1-4, 7-8, and 14 *prima facie* obvious over claims 1, 9, 13-14, 23-24, and 31-32 of copending

Application No. 10/739,750 (copending '750) in view of Gurtler et al. (U.S. Patent No. 5,773,021; "Gurtler", of record) and Mulligan et al. (U.S. Patent No. 5,128,142; "Mulligan", of record).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-4, 7-8, 10, and 13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 23, 29-31, 33, and 40-41 of copending Application No. 11/566,408 (copending '408) in view of Sikorski et al. (WO 00/38722). Independent claim 1 of the instant application has been described supra. Independent claim 23 of copending '408 claims a unitary dosage form comprising (a) a solid adsorbate comprising a low-solubility drug that is a CETPI and (b) a concentration-enhancing polymer. Dependent claim 33 of copending '408 recites many of the same properties recited in claim 10 of the instant application. Dependent claim 41 of copending '408 recites the same CETPI as required by the claims of the instant application. The primary difference between the claims is that the claims of copending '408 do not specify that the CETPI is in combination with a HMG-CoA reductase inhibitor and that the substrate has a specific surface area. This deficiency is cured by the teachings of Sikorski, which establishes that both CETPI and HMG-CoA reductase inhibitors are known to be indicated for the treatment of the same conditions and are known in combination. Regarding the surface area deficiency, it would have been prima facie obvious to optimize the substrate surface area to control and modify the bioavailability of the adsorbed drug (i.e. more surface area = higher bioavailability for a

given amorphous API). Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 1-4, 7-8, and 14 *prima facie* obvious over claims 1, 9, 13-14, 23-24, and 31-32 of copending Application No. 10/739,750 (copending '750) view of Sikorski et al. (WO 00/38722).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 7-8, and 13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6-7, 9-10, and 12-13 of copending Application No. 11/759,743 (copending '743). Independent claim 1 of the instant application has been described supra. Independent claim 1 of copending '743 claims a solid adsorbate comprising (a) a hydrophobic drug, and (b) a water immiscible lipophilic vehicle, and (c) a porous substrate. Dependent claims 6-7 and 10 specify that the hydrophobic drug is a CETPI and claim 7 identifies the CETPI required by the claims of the instant application as an example of a suitable CETPI. Dependent claims 12-13 of copending '743 recite that the dosage form comprising a solid adsorbate of claim 1 of copending '743 further comprises a HMG CoA reductase inhibitor and specifically identifies atorvastatin as a suitable comprises a HMG CoA reductase inhibitor. The primary difference between the claims is that the claims of copending '743 do not specify that the substrate has a specific surface area. This deficiency would have been considered prima facie obvious to optimize the porous substrate surface area to control and modify the bioavailability of the adsorbed drug (i.e. more surface area = higher bioavailability for a given amorphous API). Therefore, a

person of ordinary skill in the art at the time of the instant invention would have found claims 1, 7-8, and 13 *prima facie* obvious over claims 1, 6-7, 9-10, and 12-13 of copending Application No. 11/759,743 (copending '743).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Claims 1-4, 7-8, and 10-15 are rejected. Claim 3 is objected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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